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June 14, 1999Receipt #4
PATENT APPLICATION
Docket No.: KIR95-01A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Yuti Chernajovsky, Richard Neve and Marc Feldmann
Application No.: 09/285,531 Group: 1632
Filed: April 2, 1999 Examiner: Not assigned
For: SMALL MOLECULAR WEIGHT TNF RECEPTOR MULTIMERIC MOLECULE

CERTIFICATE OF MAILING	
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REQUEST FOR CORRECTED FILING RECEIPT

Customer Correction Branch
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Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

On the Filing Receipt that we received for the referenced patent application, the Filing Date is recorded incorrectly as "April 20, 1999."

This application was filed, via Express Mail procedures, on April 2, 1999. Copies of the Express Mail label, postcard receipts, and page 1 of the Specification are enclosed for the convenience of the Patent Office. Each of these clearly indicates the filing date of this application to be April 2, 1999.

Also enclosed is a copy of the Filing Receipt with the correction to the Filing Date noted in red. Please correct the Filing Date for this application in the Patent Office records and issue a Corrected Filing Receipt.

Since the error was made by the U.S. Patent and Trademark Office and not by Applicants or Applicants' Attorney, it is understood that there are no additional fees for the requested corrected Filing Receipt.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By David E. Brook

David E. Brook

Registration No.: 22,592

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Lexington, MA 02421-4799

Date: June 14, 1999

FILING RECEIPT



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APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.	DRWGS	TOT CL	IND CL
09/285,531	04/20/99	1632	\$0.00	KIR95-01A	5	14	6

04/02/99

DAVID E BROOK
HAMILTON BROOK SMITH & REYNOLDS P C
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Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Application Processing Division's Customer Correction Branch within 10 days of receipt. Please provide a copy of the Filing Receipt with the changes noted thereon.

Applicant(s)

YUTI CHERNAJOVSKY, LONDON, GREAT BRITAIN; RICHARD NEVE,
KENT, GREAT BRITAIN; MARC FELDMANN, LONDON, GREAT BRITAIN.

CONTINUING DATA AS CLAIMED BY APPLICANT-

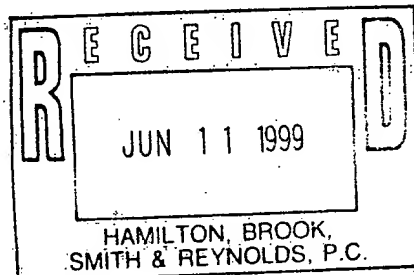
THIS APPLN IS A CON OF 08/437,533 05/09/95 ABN

IF REQUIRED, FOREIGN FILING LICENSE GRANTED 06/07/99

TITLE

SMALL MOLECULAR WEIGHT TNF RECEPTOR MULTIMERIC MOLECULE

PRELIMINARY CLASS: 435



DATA ENTRY BY: MEREDITH, WANDA

TEAM: 03 DATE: 06/07/99



(see reverse)



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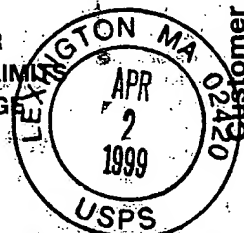
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Docket No.: KIR95-01A

April 2, 1999

This acknowledges receipt of X CONTINUATION DIVISION 53(b) as follows:
X Application Transmittal Express Mail Label No. EL192626414US
X Specification - Total pages 24
X Drawings Formal X Informal - Total sheets 5
X Copy of executed Declaration/POA from prior Application No. 08/437,533
X Information Disclosure Statement (IDS) X PTO 1449 form (2 pgs) X cited
references AA-AC: AL-AM and AR-AY
X Sequence Listing in Paper & CRF, Statement 1.821 (e) and (f)
X Other: Preliminary Amendment

jc525 U.S. PTO

09/285531

Applicant(s): Yuti Chernajovsky *et al.*

X Continuation of Application No. 08/437,533



Title: Small Molecular Weight TNF Receptor Multimeric Molecule

04/02/99

Date received by the PTO:

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Docket No.: KIR95-01A

April 2, 1999

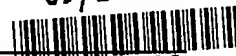
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X Other: Preliminary Amendment

jc525 U.S. PTO

09/285531

Applicant(s): Yuti Chernajovsky *et al.*

X Continuation of Application No. 08/437,533



Title: Small Molecular Weight TNF Receptor Multimeric Molecule

04/02/99

Date received by the PTO:



-1-

Date: April 2, 1999 Express Mail Label No. EL19262644US

Inventor(s): Yuti Chernajovsky, Richard Neve and Marc Feldmann

Attorney's Docket No.: KIR95-01A

COPY

Small Molecular Weight TNF Receptor Multimeric Molecule

RELATED APPLICATION(S)

This application is a Continuation of 08/437,533 filed May 9, 1995, the entire teachings of which are incorporated herein by reference.

5 BACKGROUND OF THE INVENTION

Tumor Necrosis Factor, a pleiotropic cytokine released by activated T cells and macrophages, is expressed as a mature 17 kDa protein that is active as a trimer (Smith, R.A. and Baglioni, C., *J. Biol. Chem.*, 262:6951 (1986). Trimeric cytokines such as Tumor Necrosis Factor (TNF α) and the closely related protein lymphotoxin (TNF β),
10 exert their biological activity by aggregating their cell surface receptors. The TNF trimer binds the receptors on the cell surface causing localized crosslinking of TNF receptors into clusters necessary for signal transduction.

The action of TNF α and TNF β are mediated through two cell surface receptors, the 55 kDa (p55 TNF-R) and the 75 kDa (p75 TNF-R) receptors. Truncated forms of
15 these receptors, comprising the extracellular domains (ECD) of the receptors, have been detected in the urine and serum as 30 kDa and 40 kDa TNF inhibitory binding proteins (Engelmann, H., *et al.*, *J. Biol. Chem.*, 265:1531 (1990)).

TNF is a key mediator in a number of autoimmune and inflammatory diseases such as rheumatoid arthritis, septic shock, cerebral malaria and multiple sclerosis
20 (reviewed in Tracy, K.J. and Cerami, A., *Ann. Rev. Cell. Biol.*, 9:317 (1993)).

Antagonistic TNF treatment with anti-TNF antibodies and dimeric TNF-receptor-IgG